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C_{1-6}alkyl-C_{3-8}cycloalkyl, -O-R^2, -O-C(=O)R^2, -C_{1-8}alkyl-O-R^{10}, -C_{1-8}alkyl-O-C(=O)R^{10}, -C_{1-8}alkyl-C(=O)OR^{10}, -C_{1-8}alkyl-O-C(=O)OR^{10}, -C_{1-8}alkyl-C(=O)N$R^{10}R^{10}$, -C_{1-8}alkyl-N$R^{10}R^{10}$, -C_{1-8}alkyl-NR^{10}C(=O)R^{10}, -SR^{10}, where R^2 is as described above and

R^{10} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

each R^{14} group is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, -NO_2, C_{1-8}alkyl-OH, C_{0-8}alkyl-SH, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

REMARKS

Claims 1-16 are pending in this application and presented for examination. Claims 1-2, 5, 9 and 11 have been amended. No new matter has been introduced with the foregoing amendments. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Reconsideration is respectfully requested.

I. REJECTION UNDER 35 U.S.C. § 112, second paragraph

Claims 1-16 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Each of the Examiner's concerns, and Applicants response to those concerns, will be addressed in turn.

a) With respect to the double inclusion of the variable "OH" in R^1 and R^{14}, Applicants have amended "C_0-C_6alkyl-OH" to set forth C_1-C_6alkyl-OH. As such, Applicants respectfully request that the Examiner withdraw the rejection.

b) With respect to the typographical errors of r^6 and r^{18}, Applicants have amended the claims to set forth R^6 and R^{18}. As such, Applicants respectfully request that the Examiner withdraw the rejection.

c) With respect to the term "prodrug derivatives", Applicants have deleted the term from the claims in an earnest effort to advance prosecution of the application. As such, Applicants respectfully request that the Examiner withdraw the rejection.

d) With respect to the term "containing" in the definition of "heterocycle", Applicants have followed the Examiner's suggestion and amended the claims to set forth "having". As such, Applicants respectfully request that the Examiner withdraw the rejection.

In view of the foregoing amendments, Applicants respectfully request that the Examiner withdraw the rejections under 35 U.S.C. § 112, second paragraph.

II. REJECTION UNDER 35 U.S.C. § 112, first paragraph

Claims 1-16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for the term "prodrug derivative".

In an earnest effort to advance prosecution of the application, Applicants have amended the claims to delete the term. As such, Applicants respectfully request that the Examiner withdraw the rejection.

Claims 14-15 were rejected were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for preventing a condition...characterized by undesired thrombosis. In response, Applicants respectfully traverse the rejection.

Applicants respectfully point out that the proper standard for determining whether the claims are adequately enabled is whether undue experimentation is required by one skilled in the art to practice the invention. The analysis includes consideration of

factors such as the amount of guidance provided in the application and the presence of working examples. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

In the instant case, the claims are adequately enabled for treating the various conditions and indication set forth in claims 14-15, as one of ordinary skill in the art can practice the claimed invention without undue experimentation. As set out in *Wands*, "a *considerable* amount of experimentation is permissible, if it is merely *routine*, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should precede." *In re Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982) (Emphasis added).

Clearly, in the instant application, the amount of experimentation is not undue as the specification gives adequate guidance. In this respect, the Examiner's attention is respectfully directed to page 32, lines 13-17 of the present specification, wherein it teaches:

> The biological properties of the compounds of the present invention can be readily characterized by methods that are well known in the art, for example by the *in vitro* protease activity assays and *in vivo* studies to evaluate antithrombotic efficacy, and effects on hemostasis and hematological parameters, such as are illustrated in the examples.

Specific assays both *in vivo* and *in vitro*, to teach the biological efficacy are set forth in detail on page 41, line 24, continuing to the top of page 43. For example, amidolytic assays for determining protease inhibition activity has been described. These assays include, factor Xa and thrombin assays as well as prothrombinase inhibition assays.

In addition, the antithrombotic efficacy of the compounds was assayed in a rabbit model of venous thrombosis, using a rabbit deep vein thrombosis model as described by Hollenbach, S. *et al.*, *Thromb. Haemost.* 71, 357-362 (1994), wherein the *in-vivo* antithrombotic activity of the test compounds was determined.

Further, guidance is given in the biological data table set forth on page 46. As tabulated therein, 19 compounds where tested with a battery of biological assay. Based on the evidence regarding the detailed guidance set forth above, the specification at the time the application was filed, would have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Moreover, Applicants assert that the number of working examples disclosed in the specification is sufficient to enable the full scope of the claims. Applicants are not required to disclose every type of indications within "undesired thrombosis". For example, in *In re Angstadt*, the court decided that Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art" and that "the disclosure of forty working examples sufficiently described the subject matter of claims directed to a generic process." 537 F.2d at 502-03, 190 USPQ at 218. As such, if Applicants show efficacy for the treatment of undesired thrombosis, such as with a factor Xa assay, a thrombin assay as well as prothrombinase inhibition assay, they are entitle to sub-indications within such indication.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

III. REJECTION UNDER 35 U.S.C. 102(a)

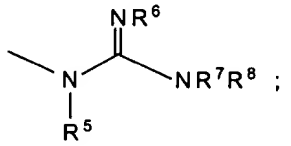
Claims 1-2 and 13-16 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by WO 99/50254 ("Dudley *et al.*"). To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

"To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter" (*see, PPG Industries Inc. v. Guardian Industries Corp.*, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996)).

Applicants have amended the structure in claim 1 to set forth quinolone derivatives. Applicants note that in no instance does Dudley *et al.* teach or suggest

quinolone derivatives *i.e.*, when "X" of the present Formula I is CR^{12}. As such, these derivatives are neither anticipated nor rendered obvious in view of Dudley *et al.*

Applicants have amended claim 2 to set forth quinoxalone derivatives, wherein "A" in Formula I, is a member selected from the following:



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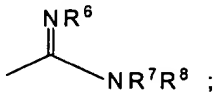

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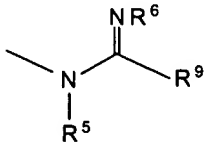
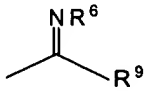


and



;

and Z is a member selected from the group of C_{1-8}alkyl, C_{3-8}cycloalkyl, and a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S;

D is a member selected from the group of a direct link, $-CH_2-$, -O-, $-N(R^2)-$, -C(=O)-, -S-, $-SO_2-$, $-SO_2-N(R^2)-$, $-N(R^2)-SO_2-$, -OC(=O)-, -C(=O)O-, $-C(=O)-N(R^2)-$ and $-N(R^2)-C(=O)-$, provided that when Z is C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{1-8}carbocyclic aryl, then D is -O-, or $-N(R^2)-$. The other variables have not been changed. This embodiment is not taught, suggested or disclosed in Dudley *et al.* As such, the instant invention is neither anticipated or rendered obvious in view of the cited art.

As such, Applicants respectfully request that the Examiner withdraw the rejection.

IV. CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925.472.5000.

Respectfully submitted,

Joseph R. Snyder
Reg. No. 39,381

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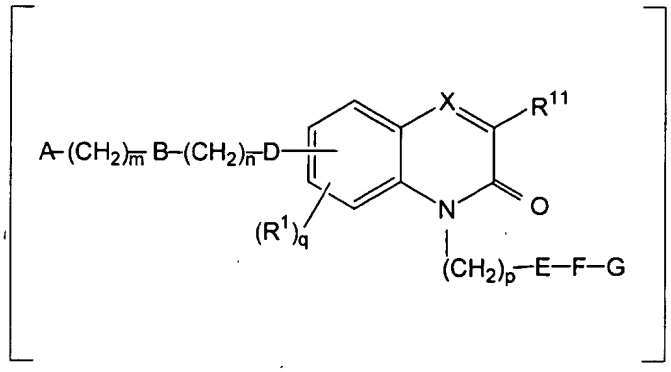
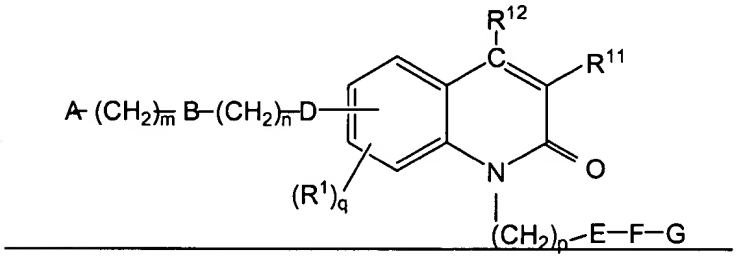
JS:js
WC 9047272 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE in Amdt A

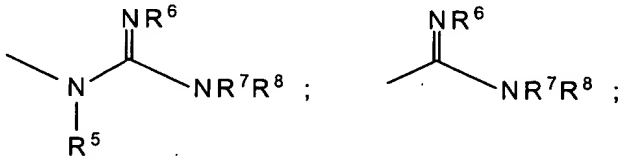
1. (Amended) A compound of having the following formula:

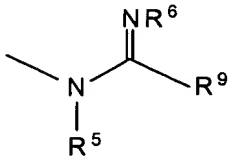




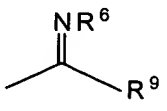
wherein:

A is a member selected from the group consisting of: R^2, $-NR^3R^4$, $-C(=O)NR^3R^4$,





and



;

where R^2, R^3, R^4, R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, -OH, $C_{1\text{-}8}$alkyl, $C_{2\text{-}8}$alkenyl, $C_{2\text{-}8}$alkynyl, $C_{3\text{-}8}$cycloalkyl, $C_{6\text{-}12}$carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4

heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where R^6 taken with either of R^7 and R^8, and/or R^7 taken with R^8, can each form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4 atoms selected from the group consisting of N, O and S;

m is an integer from 0-3;

Z is a member selected from the group consisting of a direct link, C_{1-8}alkyl, C_{3-8}cycloalkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{1-8}carbocyclic aryl, or a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S;

n is an integer from 0-3;

D is a member selected from the group consisting of a direct link, $-CH_2-$, -O-, $-N(R^2)-$, -C(=O)-, -S-, $-SO_2-$, $-SO_2-N(R^2)-$, $-N(R^2)-SO_2-$, -OC(=O)-, -C(=O)O-, -C(=O)-$N(R^2)$- and $-N(R^2)-C(=O)-$;

R^1 is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, $-NO_2$, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, $-C(=O)NR^2R^3$, $-O-R^2$ and $-O-C(=O)R^2$, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, $-SO_2R^2$, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, where R^2 and R^3 is as described above;

q is an integer from 0-3;

[X is N or $-CR^{12}$;]

R^{11} and R^{12} are independently a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, C_{1-6}alkylaryl,

C_{1-6}alkyl-C_{3-8}cycloalkyl, -O-R^2, -O-C(=O)R^2, -C_{1-8}alkyl-O-R^{10}, -C_{1-8}alkyl-O-C(=O)R^{10}, -C_{1-8}alkyl-C(=O)OR^{10}, -C_{1-8}alkyl-O-C(=O)OR^{10}, -C_{1-8}alkyl-C(=O)N$R^{10}R^{10}$, -C_{1-8}alkyl-N$R^{10}R^{10}$, -C_{1-8}alkyl-NR^{10}C(=O)R^{10}, -SR^{10}, where R^2 is as described above and R^{10} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

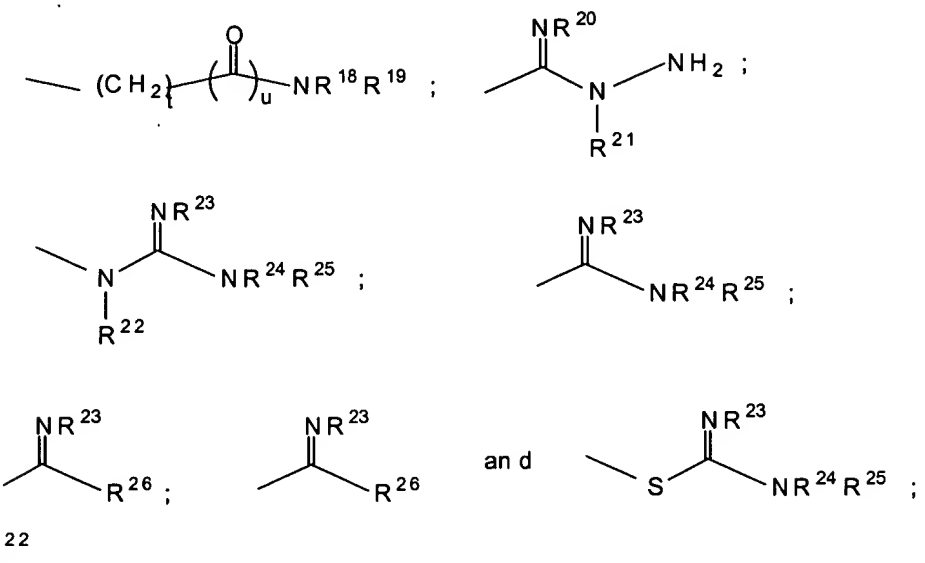
p is an integer from 0-3;

E is a member selected from the group consisting of a direct link, -O-, -N(-R^{11})- , where R^{11} is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C_{3-8}cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

each R^{14} group is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, -NO_2, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

64 G is a member selected from the group consisting of: H; -CN; -OR^{17};



65 wherein

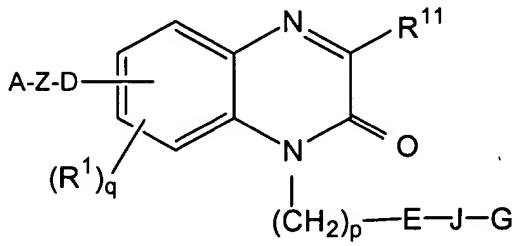
66 t is an integer from 0 to 6,

67 u is the integer 0 or 1, and R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25} and R^{26} are
68 independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring
70 system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O
71 and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with
72 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^{18}]**
73 R^{18} taken with R^{19}, R^{22} taken with either of R^{24} and R^{25}, and R^{24} taken with R^{25}, can each
74 independently form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4
75 atoms selected from the group consisting of N, O and S;

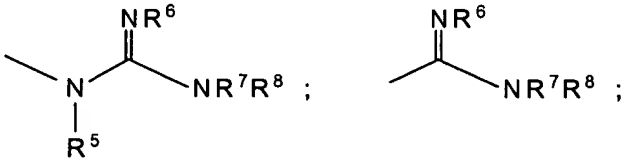
76 with the proviso that when G is H, -CN, -OR^{17}, either E or J must contain at least
77 one N atom;

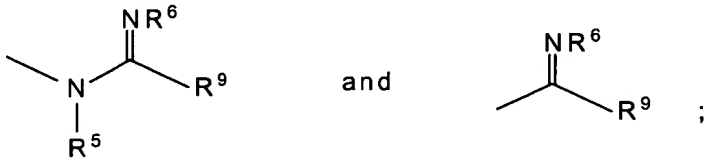
[and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof] or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

2. (Amended) A compound of formula II:



A is a member selected from the group consisting of: **[R^2, $-NR^3R^4$, $-C(=O)NR^3R^4$,]**





where **[R^2, R^3, R^4,]** R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^6]** R^6 taken with either of R^7 and R^8, and/or R^7 taken with R^8, can each form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4 atoms selected from the group consisting of N, O and S;

Z is a member selected from the group consisting of **[a direct link,]** C_{1-8}alkyl,

C_{3-8}cycloalkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{1-8}carbocyclic aryl, or a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S;

D is a member selected from the group consisting of a direct link, $-CH_2-$, -O-, $-N(R^2)-$, -C(=O)-, -S-, $-SO_2-$, $-SO_2-N(R^2)-$, $-N(R^2)-SO_2-$, -OC(=O)-, -C(=O)O-, $-C(=O)-N(R^2)-$ and $-N(R^2)-C(=O)-$ provided that when Z is C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{1-8}carbocyclic aryl, then D is -O-, or $-N(R^2)-$;

R^1 is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, $-NO_2$, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, $-C(=O)NR^2R^3$, $-O-R^2$ and $-O-C(=O)R^2$, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, $-SO_2R^2$, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, **[where R^2 and R^3 is as described above]**;

R^2, R^3 are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

q is an integer from 0-3;

R^{11} is independently a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, C_{1-6}alkylaryl, C_{1-6}alkyl-C_{3-8}cycloalkyl, $-O-R^2$, $-O-C(=O)R^2$, $-C_{1-8}$alkyl-$O-R^{10}$, $-C_{1-8}$alkyl-$O-C(=O)R^{10}$, $-C_{1-8}$alkyl-$C(=O)OR^{10}$, $-C_{1-8}$alkyl-$O-C(=O)OR^{10}$, $-C_{1-8}$alkyl-$C(=O)NR^{10}R^{10}$, $-C_{1-8}$alkyl-$NR^{10}R^{10}$, $-C_{1-8}$alkyl-$NR^{10}C(=O)R^{10}$, $-SR^{10}$, where R^2 is as described above and

R^{10} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

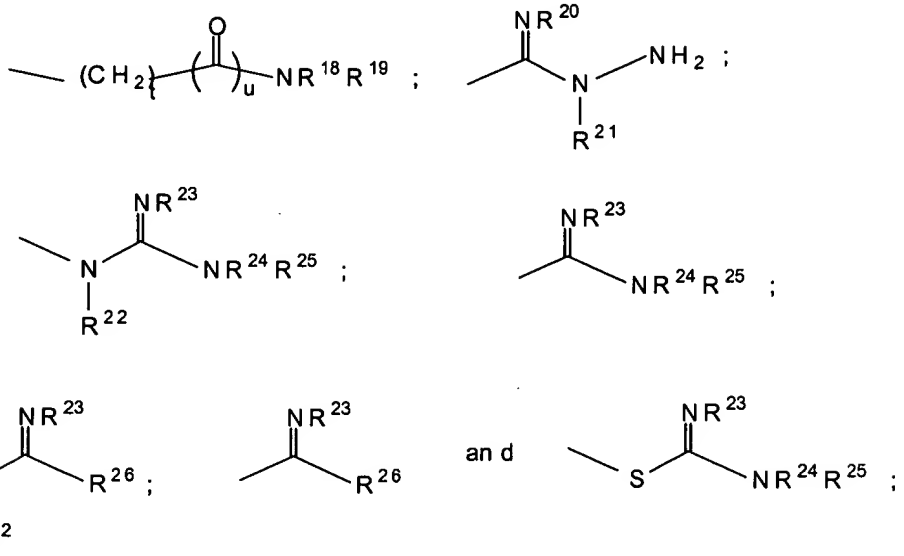
p is an integer from 0-2;

E is a member selected from the group consisting of a direct link, -O-, -N(-R^{11})- , where R^{11} is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C_{3-8}cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

each R^{14} group is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, -NO_2, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

66 G is a member selected from the group consisting of: H; -CN; -OR^{17};



67 wherein

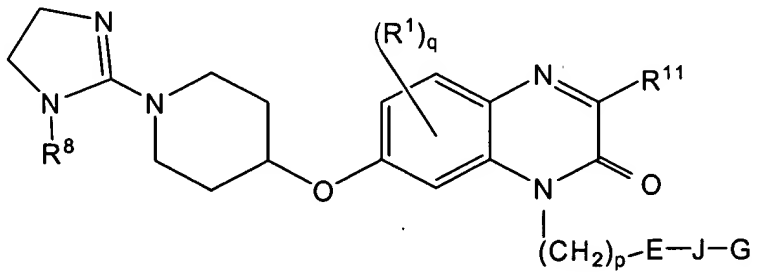
68 t is an integer from 0 to 6,

69 u is the integer 0 or 1, and R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25} and R^{26} are
70 independently selected from the group consisting of H, -OH, $C_{1\text{-}8}$alkyl, $C_{2\text{-}8}$alkenyl, $C_{2\text{-}8}$alkynyl, $C_{3\text{-}8}$cycloalkyl, $C_{6\text{-}12}$carbocyclic aryl, a five to ten membered heterocyclic ring
72 system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O
73 and S; and $C_{1\text{-}6}$alkylheterocyclic ring system having in the ring system 5 to 10 atoms with
74 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^{18}]**
75 R^{18} taken with R^{19}, R^{22} taken with either of R^{24} and R^{25}, and R^{24} taken with R^{25}, can each
76 independently form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4
77 atoms selected from the group consisting of N, O and S;

78 with the proviso that when G is H, -CN, -OR^{17}, either E or J must contain at least
79 one N atom;

[and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof] or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

5. (Amended) A compound of formula III:



(III)

wherein:

R^8 is selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

R^1 is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, -NO_2, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, -C(=O)NR^2R^3, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, -SO_2R^2, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, where R^2 and R^3 is as described above;

R^2 is selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring

system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

q is 0-3;

R^{11} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, C_{1-6}alkylaryl, C_{1-6}alkyl-C_{3-8}cycloalkyl, -O-R^2, -O-C(=O)R^2, -C_{1-8}alkyl-O-R^{10}, -C_{1-8}alkyl-O-C(=O)R^{10}, -C_{1-8}alkyl-C(=O)OR^{10}, -C_{1-8}alkyl-O-C(=O)OR^{10}, -C_{1-8}alkyl-C(=O)N$R^{10}R^{10}$, -C_{1-8}alkyl-N$R^{10}R^{10}$, -C_{1-8}alkyl-NR^{10}C(=O)R^{10}, -SR^{10}, where R^2 is as described above and R^{10} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

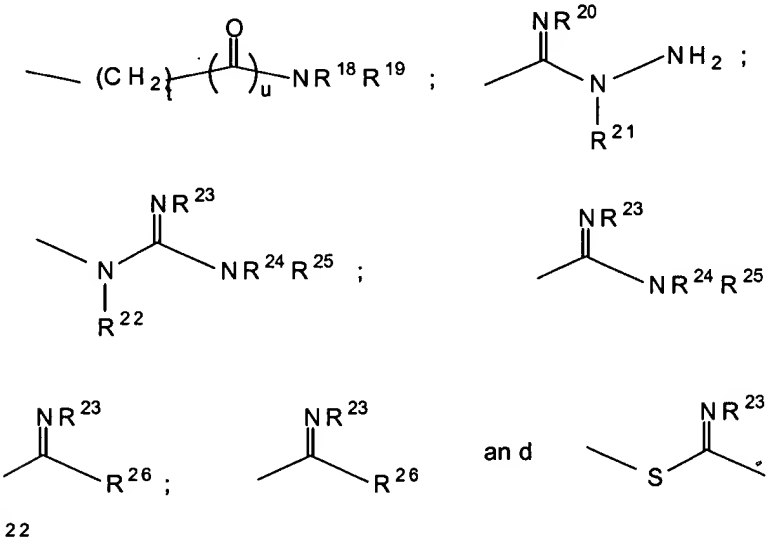
p is an integer from 0-2;

E is a member selected from the group consisting of a direct link, -O-, -N(-R^{11})- , where R^{11} is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C_{3-8}cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group **[containing]** having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

each R^{14} group is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, $-NO_2$, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

G is a member selected from the group consisting of: H; -CN; $-OR^{17}$;



wherein

t is an integer from 0 to 6,

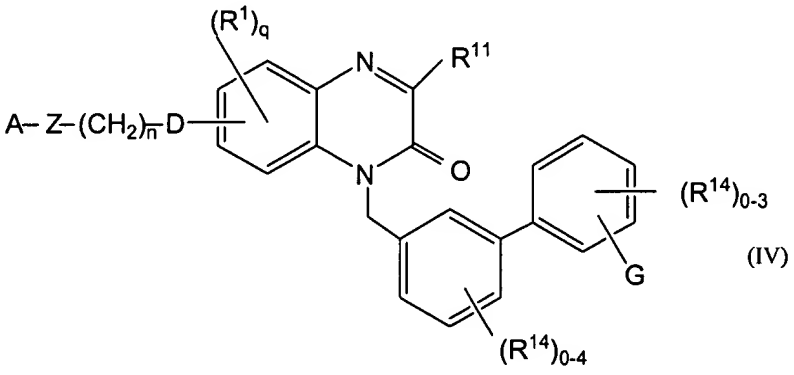
u is the integer 0 or 1, and R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25} and R^{26} are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^{18}]**

R^{18} taken with R^{19}, R^{22} taken with either of R^{24} and R^{25}, and R^{24} taken with R^{25}, can each independently form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, $-OR^{17}$, either E or J must contain at least one N atom;

[and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof] or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

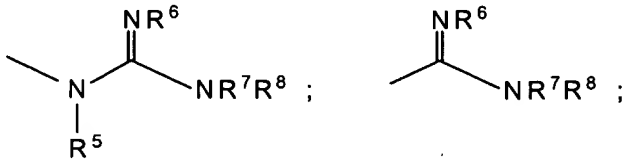
9. A compound of formula IV:

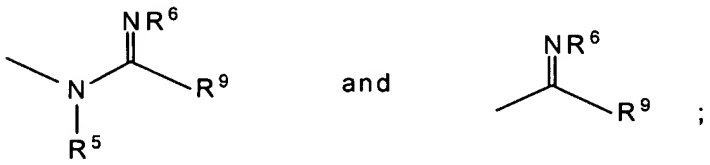


(IV)

wherein:

A is a member selected from the group consisting of: R^2, $-NR^3R^4$, $-C(=O)NR^3R^4$,





where R^2, R^3, R^4, R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic

aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^6]** R^6 taken with either of R^7 and R^8, and/or R^7 taken with R^8, can each form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4 atoms selected from the group consisting of N, O and S;

Z is a member selected from the group consisting of a direct link, C_{1-8}alkyl, C_{3-8}cycloalkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{1-8}carbocyclic aryl, or a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S;

n is 0-3;

D is a member selected from the group consisting of: $-CH_2-$, -O-, $-N\,R^2$, -C(=O)-, -S-, $-SO_2-$, $-SO_2-NR^2$, $-NR^2-SO_2$, -OC(=O)-, $-C(=O)NR^2$, and $-NR^2-C(=O)-$;

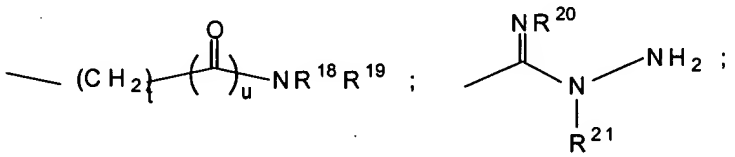
R^1 and R^{14} are independently a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, $-NO_2$, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, $-O-R^2$ and $-O-C(=O)R^2$, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

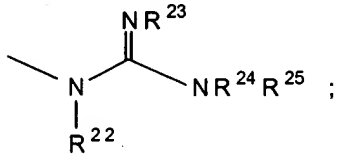
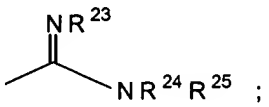
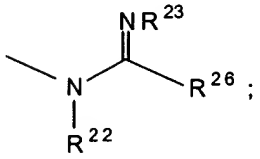
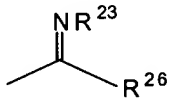
q is 0-3;

R^{11} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, C_{1-6}alkylaryl, C_{1-6}alkyl-C_{3-8}cycloalkyl, $-O-R^2$, $-O-C(=O)R^2$, $-C_{1-8}$alkyl-$O-R^{10}$, $-C_{1-8}$alkyl-$O-C(=O)R^{10}$, $-C_{1-8}$alkyl-$C(=O)OR^{10}$, $-C_{1-8}$alkyl-$O-C(=O)OR^{10}$, $-C_{1-8}$alkyl-$C(=O)NR^{10}R^{10}$, $-C_{1-8}$alkyl-$NR^{10}R^{10}$, $-C_{1-8}$alkyl-$NR^{10}C(=O)R^{10}$, $-SR^{10}$, where R^2 is as described above and R^{10} is a member

selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

G is a member selected from the group consisting of: H; -CN; -OR^{17};

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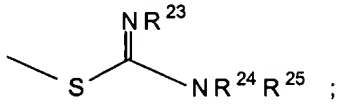


wherein

t is an integer from 0 to 6,

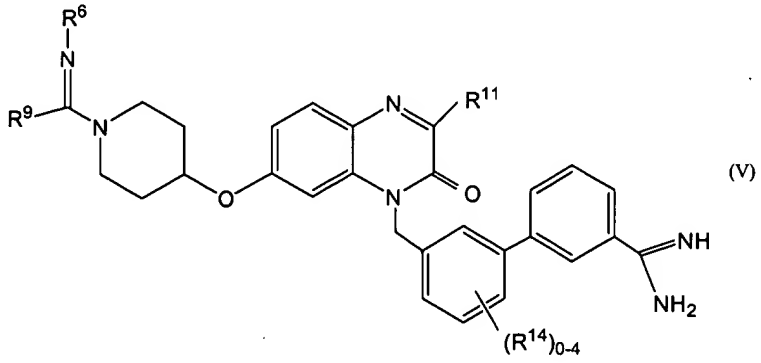
u is the integer 0 or 1, and R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25} and R^{26} are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where **[r^{18}]** R^{18} taken with R^{19}, R^{22} taken with either of R^{24} and R^{25}, and R^{24} taken with R^{25}, can each independently form a 5 to 6 membered heterocyclic ring **[containing]** having from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, -OR^{17}, either E or J must contain at least

one N atom;

[and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof] or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

11. A compound of formula V:



(V)

wherein:

R^2, R^6, and R^9 are independently selected from the group consisting of H, -OH, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, a five to ten membered heterocyclic ring system **[containing]** having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

R^{11} is independently a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, C_{6-12}carbocyclic aryl, C_{1-6}alkylaryl, C_{1-6}alkyl-C_{3-8}cycloalkyl, -O-R^2, -O-C(=O)R^2, -C_{1-8}alkyl-O-R^{10}, -C_{1-8}alkyl-O-C(=O)R^{10}, -C_{1-8}alkyl-C(=O)OR^{10}, -C_{1-8}alkyl-O-C(=O)OR^{10}, -C_{1-8}alkyl-C(=O)N$R^{10}R^{10}$, -C_{1-8}alkyl-N$R^{10}R^{10}$, -C_{1-8}alkyl-NR^{10}C(=O)R^{10}, -SR^{10}, where R^2 is as described above and R^{10} is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, and wherein when two R^{10} groups are present they may be taken together to

form a saturated or unsaturated ring with the atom to which they are both attached;

each R^{14} group is a member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, halogen, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH, C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl, -CN, -NO_2, **[C_{0-8}alkyl-OH,]** C_1-C_6alkyl-OH, C_{0-8}alkyl-SH, -O-R^2 and -O-C(=O)R^2, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, C_{3-8}cycloalkyl, polyhaloalkyl, C_{0-8}alkyl-C(=O)OH and C_{0-8}alkyl-C(=O)O-C_{1-8}alkyl;

[and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof] or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.